```
=> d his full

     (FILE 'HOME' ENTERED AT 11:19:26 ON 17 JUN 2005)

     FILE 'CAPLUS' ENTERED AT 11:20:43 ON 17 JUN 2005
                SET LINE 250
                SET DETAIL OFF
                E US2003-658989/AP,PRN 25.
                SET NOTICE 1000 SEARCH
L1            1 SEA ABB=ON  US2003-658989/AP
                SET NOTICE LOGIN SEARCH
                SET LINE LOGIN
                SET DETAIL LOGIN
                D SCAN
L2         1756 SEA ABB=ON  PLASMA/OBI(L)EXPANDER#/OBI
L3          175 SEA ABB=ON  GELATIN#/OBI(L)LIKE/OBI
L4        28541 SEA ABB=ON  RECOMB?/OBI(L)PROTEIN#/OBI
L5        23678 SEA ABB=ON  OSMOTIC?/OBI
L6         3359 SEA ABB=ON  PHYSIOLOGIC?/OBI(L)SALINE/OBI
L7            9 SEA ABB=ON  L3 AND (L2 OR (L4 OR L5 OR L6))
                D SCAN TI
                D SCAN

     FILE 'STNGUIDE' ENTERED AT 11:25:22 ON 17 JUN 2005

     FILE 'CAPLUS' ENTERED AT 11:27:01 ON 17 JUN 2005
L8           24 SEA ABB=ON  GELATIN#/OBI(W)LIKE/OBI
L9        44086 SEA ABB=ON  COLLOID#/OBI
L10        2310 SEA ABB=ON  BLOOD SUBSTITUTES/CT
L11           8 SEA ABB=ON  L8 AND (L2 OR (L4 OR L5 OR L6) OR (L9 OR L10))
                D SCAN TI
L12           2 SEA ABB=ON  ORGANIC/TI AND L11
                D SCAN
L13        2602 SEA ABB=ON  PLASMA/OBI(L)SUBSTITUT?/OBI
L14           8 SEA ABB=ON  L8 AND (L2 OR (L4 OR L5 OR L6) OR (L9 OR L10) OR
                L13)
L15       57867 SEA ABB=ON  (ISOELEC?)/BI
L16      665731 SEA ABB=ON  (MW OR MOLEC?(W)WEIGHT OR KDA OR KILODALTON# OR
                DALTON#)/BI
L17           6 SEA ABB=ON  L8 AND (L15 OR L16)
L18           1 SEA ABB=ON  L17 NOT L14
                D KWIC
L19       63402 SEA ABB=ON  COLLAGEN#/OBI
L20           1 SEA ABB=ON  L19 AND L4 AND (L2 OR L5 OR L6 OR L9 OR L10 OR
                L13)
                D SCAN
L21          74 SEA ABB=ON  RECOMB?/OBI(L)GELATIN#/OBI
L22           4 SEA ABB=ON  L21 AND (L2 OR L5 OR L6 OR L9 OR L10 OR L13)
                D SCAN L22

     INDEX '1MOBILITY, 2MOBILITY, ABI-INFORM, ADISCTI, AEROSPACE, AGRICOLA,
     ALUMINIUM, ANABSTR, ANTE, APOLLIT, AQUALINE, AQUASCI, AQUIRE, BABS,
     BIBLIODATA, BIOBUSINESS, BIOCOMMERCE, BIOENG, BIOSIS, BIOTECHABS,
     BIOTECHDS, BIOTECHNO, BLLDB, CABA, CANCERLIT, ...' ENTERED AT 11:34:57 ON
     17 JUN 2005
                SEA (GELATIN# OR COLLAGEN#)(3A)(LIKE OR RECOMB?)
               ---------
              30   FILE ABI-INFORM
              17   FILE ADISCTI
               3   FILE AEROSPACE
```

33 FILE AGRICOLA
4 FILE ANABSTR
12 FILE ANTE
21 FILE APOLLIT
56 FILE AQUASCI
33 FILE BABS
8 FILE BIBLIODATA
42 FILE BIOBUSINESS
20 FILE BIOCOMMERCE
96 FILE BIOENG
1885 FILE BIOSIS
173 FILE BIOTECHABS
173 FILE BIOTECHDS
679 FILE BIOTECHNO
127 FILE CABA
281 FILE CANCERLIT
3 FILE CAOLD
904 FILE CAPLUS
2 FILE CASREACT
30 FILE CBNB
16 FILE CEABA-VTB
2 FILE CEN
5 FILE CERAB
41 FILE CIN
2 FILE CIVILENG
174 FILE COMPENDEX
1 FILE COMPUAB
36 FILE CONFSCI
1 FILE COPPERLIT
1 FILE CROPU
2 FILE CSNB
32 FILE DDFB
48 FILE DDFU
1521 FILE DGENE
105 FILE DISSABS
69 FILE DPCI
32 FILE DRUGB
76 FILE DRUGU
7 FILE EMA
14 FILE EMBAL
1509 FILE EMBASE
1 FILE ENCOMPLIT
1 FILE ENCOMPPAT
27 FILE ENERGY
1 FILE ENTEC
2447 FILE EPFULL
680 FILE ESBIOBASE
7 FILE FRFULL
37 FILE FROSTI
39 FILE FSTA
274 FILE GBFULL
648 FILE GENBANK
4 FILE GEOREF
294 FILE IFIPAT
8 FILE IMSDRUGNEWS
15 FILE INIS
311 FILE INPADOC
71 FILE INSPEC
7 FILE INSPHYS
59 FILE INVESTEXT

```
             7   FILE IPA
           294   FILE JAPIO
           240   FILE JICST-EPLUS
             7   FILE KOREAPAT
            14   FILE KOSMET
           471   FILE LIFESCI
             1   FILE MATBUS
             3   FILE MECHENG
          1671   FILE MEDLINE
             3   FILE METADEX
             2   FILE NAPRALERT
             6   FILE NIOSHTIC
           118   FILE NLDB
            15   FILE NTIS
            11   FILE OCEAN
            10   FILE PAPERCHEM2
           502   FILE PASCAL
             4   FILE PATDPAFULL
          2792   FILE PCTFULL
             2   FILE PHARMAML
            23   FILE PHIN
             7   FILE PIRA
             1   FILE POLLUAB
           327   FILE PROMT
            13   FILE RAPRA
          1533   FILE SCISEARCH
             1   FILE SOLIDSTATE
            42   FILE TEMA
             3   FILE TEXTILETECH
           531   FILE TOXCENTER
             1   FILE TULSA
          8787   FILE USPATFULL
           712   FILE USPAT2
             2   FILE VETU
           374   FILE WPIDS
           374   FILE WPINDEX
             2   FILE WSCA
             8   FILE WTEXTILES
L23           QUE ABB=ON  (GELATIN# OR COLLAGEN#)(3A)(LIKE OR RECOMB?)
              ---------
              D RANK

    FILE 'STNGUIDE' ENTERED AT 11:38:43 ON 17 JUN 2005

    FILE 'JICST-EPLUS, PASCAL, CABA, BIOTECHNO, ESBIOBASE, BIOSIS, CONFSCI,
    LIFESCI, BIOTECHDS, DISSABS, BIOENG, TOXCENTER, WPIDS, SCISEARCH, DGENE'
    ENTERED AT 11:42:19 ON 17 JUN 2005
L24        86352 SEA ABB=ON  GELATIN#
L25          184 SEA ABB=ON  GELATIN#(W) LIKE
L26       403449 SEA ABB=ON  COLLAGEN#
L27        25915 SEA ABB=ON  (PLASMA OR BLOOD)(2A)(EXPAN? OR SUBSTITUT?)
L28      2587443 SEA ABB=ON  RECOMB?
L29       318738 SEA ABB=ON  OSMOTIC?
L30       380874 SEA ABB=ON  SALINE
L31       191179 SEA ABB=ON  COLLOID?
L32           72 SEA ABB=ON  L25 AND (L27 OR L28 OR L29 OR L30 OR L31)
L33           68 DUP REM L32 (4 DUPLICATES REMOVED)
                 ANSWERS '1-4' FROM FILE BIOTECHDS
                 ANSWERS '5-6' FROM FILE TOXCENTER
                 ANSWERS '7-15' FROM FILE WPIDS
```

```
                    ANSWER '16' FROM FILE SCISEARCH
                    ANSWERS '17-68' FROM FILE DGENE
L34          21 SEA ABB=ON  L25 AND L28 AND (L27 OR (L29 OR L30 OR L31))

     FILE 'JICST-EPLUS, PASCAL, CABA, BIOTECHNO, ESBIOBASE, BIOSIS, CONFSCI,
     LIFESCI, BIOTECHDS, DISSABS, BIOENG, TOXCENTER, WPIDS, SCISEARCH, DGENE'
     ENTERED AT 11:46:29 ON 17 JUN 2005

     FILE 'JICST-EPLUS, PASCAL, CABA, BIOTECHNO, ESBIOBASE, BIOSIS, CONFSCI,
     LIFESCI, BIOTECHDS, DISSABS, BIOENG, TOXCENTER, WPIDS, SCISEARCH' ENTERED
     AT 11:46:36 ON 17 JUN 2005
L35         122 SEA ABB=ON  GELATIN#(W) LIKE     .
L36       85241 SEA ABB=ON  GELATIN#
L37      384805 SEA ABB=ON  COLLAGEN#
L38     1282106 SEA ABB=ON  RECOMB?
L39       25282 SEA ABB=ON  (PLASMA OR BLOOD)(2A)(EXPAN? OR SUBSTITUT?)
L40      191497 SEA ABB=ON  OSMOTIC? OR OSMOSIS
L41      379735 SEA ABB=ON  SALINE
L42      190067 SEA ABB=ON  COLLOID?
L43           4 SEA ABB=ON  L35 AND L38 AND (L39 OR L40 OR L41 OR L42)
L44           3 SEA ABB=ON  L35 AND L39 AND (L38 OR (L40 OR L41 OR L42))
L45          26 SEA ABB=ON  (L36 OR L37) (5A) L38 AND (L39 OR L40 OR L41 OR
                  L42)
L46          21 DUP REM L45 (5 DUPLICATES REMOVED)
                    ANSWER '1' FROM FILE PASCAL
                    ANSWERS '2-6' FROM FILE BIOSIS
                    ANSWERS '7-9' FROM FILE BIOTECHDS
                    ANSWER '10' FROM FILE TOXCENTER
                    ANSWERS '11-20' FROM FILE WPIDS
                    ANSWER '21' FROM FILE SCISEARCH
                  D SCAN
                  D QUE
L47           7 SEA ABB=ON  (L36 OR L37) (5A) L38 AND L39
L48           3 SEA ABB=ON  (L36 OR L37) (5A) L38 AND L40 AND L41
L49           3 SEA ABB=ON  (L36 OR L37) (5A) L38 AND L40 AND L42
                  D SCAN L48
L50           3 SEA ABB=ON  L48 AND L49
L51           3 SEA ABB=ON  (L36 OR L37) (5A) L38 AND L40 AND (L41 OR L42)
L52          22 SEA ABB=ON  L45 NOT L43
L53          23 SEA ABB=ON  L45 NOT L44
L54          19 SEA ABB=ON  L45 NOT L47
L55          23 SEA ABB=ON  L45 NOT L51
L56          23 SEA ABB=ON  (L52 OR L53 OR L54 OR L55)
L57          18 DUP REM L56 (5 DUPLICATES REMOVED)
                    ANSWER '1' FROM FILE PASCAL
                    ANSWERS '2-6' FROM FILE BIOSIS
                    ANSWERS '7-9' FROM FILE BIOTECHDS
                    ANSWER '10' FROM FILE TOXCENTER
                    ANSWERS '11-17' FROM FILE WPIDS
                    ANSWER '18' FROM FILE SCISEARCH
                  D SCAN
L58           4 SEA ABB=ON  L45 AND (GLYCOL OR PHARMACEUTICAL# OR BEAD OR
                  DRUG#)/TI

     FILE 'MEDLINE' ENTERED AT 11:59:24 ON 17 JUN 2005
L59          12 SEA ABB=ON  GELATIN-LIKE
L60       10666 SEA ABB=ON  (PLASMA OR BLOOD)(2A)(EXPAN? OR SUBSTITUT?)
                  D TRIAL 10000-10005
                  D TRIAL 1000-1005
                  E PLASMA SUBSTITUTES+ALL/CT
```

```
L61        6930 SEA ABB=ON  BLOOD SUBSTITUTES/CT OR PLASMA SUBSTITUTES/CT
                E HEMODILUTION+ALL/CT
L62        2808 SEA ABB=ON  HEMODILUTION/CT
                E GELATIN+ALL/CT
L63        5041 SEA ABB=ON  GELATIN/CT
                E RECOMB/CT
                E E14+ALL
                E E4+ALL
L64      109664 SEA ABB=ON  RECOMBINANT PROTEINS/CT
L65           0 SEA ABB=ON  L59 AND ((L60 OR L61 OR L62) OR L64)
L66           0 SEA ABB=ON  L63 AND L64 AND (L60 OR L61 OR L62)
L67          76 SEA ABB=ON  L63 AND L64
L68          46 SEA ABB=ON  L63(L)AA/CT
L69           0 SEA ABB=ON  L68 AND L64
                D TRIAL L67 1-10
                D QUE L67
L70          19 SEA ABB=ON  L63/MAJ AND L64
                D TRIAL 1-19
                D QUE
L71           2 SEA ABB=ON  L64(L)BI/CT AND L63/MAJ

     FILE 'EMBASE' ENTERED AT 12:08:43 ON 17 JUN 2005
                E BLOOD SUBSTITUTE/CT
                E E3+ALL
L72         742 SEA ABB=ON  BLOOD SUBSTITUTE/CT
                E PLASMA SUB/CT
                E E5+ALL
L73        1594 SEA ABB=ON  PLASMA SUBSTITUTE/CT
L74         259 SEA ABB=ON  ARTIFICIAL BLOOD/CT
L75           9 SEA ABB=ON  GELATIN LIKE
                D TRIAL 1-9
                D KWIC 1-3
                E GELATIN/CT
L76        5803 SEA ABB=ON  GELATIN/CT
                E E3+ALL
                E RECOMBINANT/CT
L77         154 SEA ABB=ON  RECOMBINANT/CT
                E RECOMBINANT PRO/CT
                E RECOMBINANT PROT/CT
                E RECOMBINANT PROTEIN/CT
                E E3+ALL
L78       17627 SEA ABB=ON  RECOMBINANT PROTEIN/CT
L79          37 SEA ABB=ON  L76 AND (L77 OR L78)
L80           0 SEA ABB=ON  L76 AND (L77 OR L78) AND (L72 OR L73 OR L74)
L81         273 SEA ABB=ON  L76 AND (L72 OR L73 OR L74)
L82          37 SEA ABB=ON  L76 AND (L77 OR L78)
                D TRIAL 1-10
L83           0 SEA ABB=ON  L76/MAJ AND L77
L84           9 SEA ABB=ON  L76/MAJ AND (L77 OR L78)
L85           7 SEA ABB=ON  (L77/MAJ OR L78/MAJ) AND L76
L86          14 SEA ABB=ON  L84 OR L85
                D TRIAL 1-14
L87           2 SEA ABB=ON  L84 AND L85
L88           5 SEA ABB=ON  L86 AND (PICHIA OR HYDROGEL#)
                D TRIAL 1-5
L89           3 SEA ABB=ON  L86 AND (PICHIA)

     FILE 'STNGUIDE' ENTERED AT 12:18:58 ON 17 JUN 2005

     FILE 'JICST-EPLUS, PASCAL, CABA, BIOTECHNO, ESBIOBASE, BIOSIS, CONFSCI,
```

LIFESCI, BIOTECHDS, DISSABS, BIOENG, TOXCENTER, WPIDS, SCISEARCH' ENTERED AT 12:20:44 ON 17 JUN 2005

D QUE L43
D QUE L44
D QUE L47
D QUE L51
D QUE L58

L90 9 SEA ABB=ON L43 OR L44 OR L47 OR L51 OR L58

FILE 'CAPLUS' ENTERED AT 12:20:55 ON 17 JUN 2005

D QUE L14
D QUE L20
D QUE L22

L91 9 SEA ABB=ON L14 OR L20 OR L22

FILE 'EMBASE' ENTERED AT 12:20:57 ON 17 JUN 2005

D QUE L87
D QUE L89

L92 4 SEA ABB=ON L87 OR L89

FILE 'MEDLINE' ENTERED AT 12:20:59 ON 17 JUN 2005

D QUE L65
D QUE L66
D QUE L71

FILE 'STNGUIDE' ENTERED AT 12:21:07 ON 17 JUN 2005

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS, BIOTECHDS, WPIDS' ENTERED AT 12:21:35 ON 17 JUN 2005

L93 17 DUP REM L71 L91 L92 L90 (7 DUPLICATES REMOVED)
ANSWERS '1-2' FROM FILE MEDLINE
ANSWERS '3-11' FROM FILE CAPLUS
ANSWERS '12-13' FROM FILE EMBASE
ANSWERS '14-15' FROM FILE BIOSIS
ANSWER '16' FROM FILE BIOTECHDS
ANSWER '17' FROM FILE WPIDS

D IALL 1-2
D IBIB ED ABS HITIND 3-11
D IALL 12-17

FILE 'HOME' ENTERED AT 12:22:04 ON 17 JUN 2005

FILE HOME

FILE CAPLUS

FILE COVERS 1907 - 17 Jun 2005 VOL 142 ISS 26
FILE LAST UPDATED: 16 Jun 2005 (20050616/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE STNGUIDE
FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Jun 10, 2005 (20050610/UP).

FILE STNINDEX

FILE JICST-EPLUS
FILE COVERS 1985 TO 13 JUN 2005 (20050613/ED)

THE JICST-EPLUS FILE HAS BEEN RELOADED TO REFLECT THE 1999 CONTROLLED TERM (/CT) THESAURUS RELOAD.

FILE PASCAL
FILE LAST UPDATED: 13 JUN 2005 <20050613/UP>
FILE COVERS 1977 TO DATE.

>>> SIMULTANEOUS LEFT AND RIGHT TRUNCATION IS AVAILABLE IN THE BASIC INDEX (/BI) FIELD <<<

FILE CABA
FILE COVERS 1973 TO 9 Jun 2005 (20050609/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

The CABA file was reloaded 7 December 2003. Enter HELP RLOAD for details.

FILE BIOTECHNO
FILE LAST UPDATED: 7 JAN 2004 <20040107/UP>
FILE COVERS 1980 TO 2003.

>>> BIOTECHNO IS NO LONGER BEING UPDATED AS OF 2004 <<<

>>> SIMULTANEOUS LEFT AND RIGHT TRUNCATION AVAILABLE IN /CT AND BASIC INDEX <<<

FILE ESBIOBASE
FILE LAST UPDATED: 14 JUN 2005 <20050614/UP>
FILE COVERS 1994 TO DATE.

>>> SIMULTANEOUS LEFT AND RIGHT TRUNCATION AVAILABLE IN /CC, /ORGN, AND /ST <<<

FILE BIOSIS
FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 16 June 2005 (20050616/ED)

FILE RELOADED: 19 October 2003.

FILE CONFSCI
FILE COVERS 1973 TO 25 May 2005 (20050525/ED)

FILE LIFESCI
FILE COVERS 1978 TO 16 Jun 2005 (20050616/ED)

FILE BIOTECHDS
FILE LAST UPDATED: 17 JUN 2005 <20050617/UP>

>>> USE OF THIS FILE IS LIMITED TO BIOTECH SUBSCRIBERS <<<

>>> NEW CLASSIFICATION SYSTEM FROM 2002 ONWARDS - SEE HELP CLA <<<

>>> NEW DISPLAY FIELDS LS AND LS2 (LEGAL STATUS DATA FROM
THE INPADOC DATABASE) AVAILABLE - SEE NEWS <<<

FILE DISSABS
FILE COVERS 1861 TO 25 MAY 2005 (20050525/ED)

FILE BIOENG
FILE LAST UPDATED: 18 MAY 2005 <20050518/UP>
FILE COVERS 1982 TO DATE

>>> SIMULTANEOUS LEFT AND RIGHT TRUNCATION AVAILABLE IN
THE BASIC INDEX <<<

FILE TOXCENTER

FILE COVERS 1907 TO 14 Jun 2005 (20050614/ED)

This file contains CAS Registry Numbers for easy and accurate substance
identification.

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TOXCENTER has been enhanced with new files segments and search fields.
See HELP CONTENT for more information.

TOXCENTER thesauri in the /CN, /CT, and /MN fields incorporate the
MeSH 2005 vocabulary. See http://www.nlm.nih.gov/mesh/ and
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html for a
description of changes.

FILE WPIDS
FILE LAST UPDATED: 16 JUN 2005 <20050616/UP>
MOST RECENT DERWENT UPDATE: 200538 <200538/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
PLEASE VISIT:
http://www.stn-international.de/training_center/patents/stn_guide.pdf <<<

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
http://thomsonderwent.com/coverage/latestupdates/ <<<

>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER
GUIDES, PLEASE VISIT:
http://thomsonderwent.com/support/userguides/ <<<

>>> NEW! FAST-ALERTING ACCESS TO NEWLY-PUBLISHED PATENT
DOCUMENTATION NOW AVAILABLE IN DERWENT WORLD PATENTS INDEX
FIRST VIEW - FILE WPIFV.
FOR FURTHER DETAILS: http://www.thomsonderwent.com/dwpifv <<<

>>> THE CPI AND EPI MANUAL CODES HAVE BEEN REVISED FROM UPDATE 200501.
PLEASE CHECK:
http://thomsonderwent.com/support/dwpiref/reftools/classification/code-rev
FOR DETAILS. <<<

FILE SCISEARCH
FILE COVERS 1974 TO 16 Jun 2005 (20050616/ED)

FILE DGENE
FILE LAST UPDATED: 7 JUN 2005 <20050607/UP>

DGENE CURRENTLY CONTAINS 7,111,894 BIOSEQUENCES

>>> NEW DISPLAY FIELDS LS AND LS2 (LEGAL STATUS DATA FROM
THE INPADOC DATABASE) AVAILABLE IN DGENE - SEE NEWS <<<

>>> ONLINE THESAURUS AVAILABLE IN /PACO <<<

>>> DOWNLOAD THE DGENE WORKSHOP MANUAL:
http://www.stn-international.de/training_center/bioseq/dgene_wm.pdf

>>> DOWNLOAD COMPLETE DGENE HELP AS PDF:
http://www.stn-international.de/training_center/bioseq/dgene_help.pdf <<

>>> DOWNLOAD DGENE BLAST/GETSIM FREQUENTLY ASKED QUESTIONS:
http://www.stn-international.de/service/faq/dgenefaq.pdf <<<

FILE MEDLINE
FILE LAST UPDATED: 16 JUN 2005 (20050616/UP). FILE COVERS 1950 TO DATE.

On December 19, 2004, the 2005 MeSH terms were loaded.

The MEDLINE reload for 2005 is now available. For details enter HELP
RLOAD at an arrow promt (=>). See also:

http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html

OLDMEDLINE now back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
MeSH 2005 vocabulary.

This file contains CAS Registry Numbers for easy and accurate
substance identification.

FILE EMBASE
FILE COVERS 1974 TO 16 Jun 2005 (20050616/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=>

```
=> fil JICST-EPLUS, PASCAL, CABA, BIOTECHNO, ESBIOBASE, BIOSIS, CONFSCI, LIFESCI,
BIOTECHDS, DISSABS, BIOENG, TOXCENTER, WPIDS, SCISEARCH
FILE 'JICST-EPLUS' ENTERED AT 12:20:44 ON 17 JUN 2005
COPYRIGHT (C) 2005 Japan Science and Technology Agency (JST)

FILE 'PASCAL' ENTERED AT 12:20:44 ON 17 JUN 2005
Any reproduction or dissemination in part or in full,
by means of any process and on any support whatsoever
is prohibited without the prior written agreement of INIST-CNRS.
COPYRIGHT (C) 2005 INIST-CNRS. All rights reserved.

FILE 'CABA' ENTERED AT 12:20:44 ON 17 JUN 2005
COPYRIGHT (C) 2005 CAB INTERNATIONAL (CABI)

FILE 'BIOTECHNO' ENTERED AT 12:20:44 ON 17 JUN 2005
COPYRIGHT (C) 2005 Elsevier Science B.V., Amsterdam. All rights reserved.

FILE 'ESBIOBASE' ENTERED AT 12:20:44 ON 17 JUN 2005
COPYRIGHT (C) 2005 Elsevier Science B.V., Amsterdam. All rights reserved.

FILE 'BIOSIS' ENTERED AT 12:20:44 ON 17 JUN 2005
Copyright (c) 2005 The Thomson Corporation

FILE 'CONFSCI' ENTERED AT 12:20:44 ON 17 JUN 2005
COPYRIGHT (C) 2005 Cambridge Scientific Abstracts (CSA)

FILE 'LIFESCI' ENTERED AT 12:20:44 ON 17 JUN 2005
COPYRIGHT (C) 2005 Cambridge Scientific Abstracts (CSA)


FILE 'BIOTECHDS' ENTERED AT 12:20:44 ON 17 JUN 2005
COPYRIGHT (C) 2005 THE THOMSON CORPORATION

FILE 'DISSABS' ENTERED AT 12:20:44 ON 17 JUN 2005
COPYRIGHT (C) 2005 ProQuest Information and Learning Company; All Rights Reserved.

FILE 'BIOENG' ENTERED AT 12:20:44 ON 17 JUN 2005
COPYRIGHT (C) 2005 Cambridge Scientific Abstracts (CSA)

FILE 'TOXCENTER' ENTERED AT 12:20:44 ON 17 JUN 2005
COPYRIGHT (C) 2005 ACS

FILE 'WPIDS' ENTERED AT 12:20:44 ON 17 JUN 2005
COPYRIGHT (C) 2005 THE THOMSON CORPORATION

FILE 'SCISEARCH' ENTERED AT 12:20:44 ON 17 JUN 2005
Copyright (c) 2005 The Thomson Corporation

=> d que l43; d que l44; d que l47; d que l51; d que l58

L35          122 SEA GELATIN#(W) LIKE
L38      1282106 SEA RECOMB?
L39        25282 SEA (PLASMA OR BLOOD)(2A)(EXPAN? OR SUBSTITUT?)
L40       191497 SEA OSMOTIC? OR OSMOSIS
L41       379735 SEA SALINE
L42       190067 SEA COLLOID?
L43            4 SEA L35 AND L38 AND (L39 OR L40 OR L41 OR L42)
```

```
L35         122 SEA GELATIN#(W) LIKE
L38     1282106 SEA RECOMB?
L39       25282 SEA (PLASMA OR BLOOD)(2A)(EXPAN? OR SUBSTITUT?)
L40      191497 SEA OSMOTIC? OR OSMOSIS
L41      379735 SEA SALINE
L42      190067 SEA COLLOID?
L44           3 SEA L35 AND L39 AND (L38 OR (L40 OR L41 OR L42))


L36       85241 SEA GELATIN#
L37      384805 SEA COLLAGEN#
L38     1282106 SEA RECOMB?
L39       25282 SEA (PLASMA OR BLOOD)(2A)(EXPAN? OR SUBSTITUT?)
L47           7 SEA (L36 OR L37) (5A) L38 AND L39


L36       85241 SEA GELATIN#
L37      384805 SEA COLLAGEN#
L38     1282106 SEA RECOMB?
L40      191497 SEA OSMOTIC? OR OSMOSIS
L41      379735 SEA SALINE
L42      190067 SEA COLLOID?
L51           3 SEA (L36 OR L37) (5A) L38 AND L40 AND (L41 OR L42)


L36       85241 SEA GELATIN#
L37      384805 SEA COLLAGEN#
L38     1282106 SEA RECOMB?
L39       25282 SEA (PLASMA OR BLOOD)(2A)(EXPAN? OR SUBSTITUT?)
L40      191497 SEA OSMOTIC? OR OSMOSIS
L41      379735 SEA SALINE
L42      190067 SEA COLLOID?
L45          26 SEA (L36 OR L37) (5A) L38 AND (L39 OR L40 OR L41 OR L42)
L58           4 SEA L45 AND (GLYCOL OR PHARMACEUTICAL# OR BEAD OR DRUG#)/TI


=> s l43 or l44 or l47 or l51 or l58

L90           9 L43 OR L44 OR L47 OR L51 OR L58

=> fil capl; d que l14; d que l20; d que l22

FILE 'CAPLUS' ENTERED AT 12:20:55 ON 17 JUN 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)
```

FILE COVERS 1907 - 17 Jun 2005 VOL 142 ISS 26
FILE LAST UPDATED: 16 Jun 2005 (20050616/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.
'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

L2	1756	SEA FILE=CAPLUS ABB=ON	PLASMA/OBI(L)EXPANDER#/OBI
L4	28541	SEA FILE=CAPLUS ABB=ON	RECOMB?/OBI(L)PROTEIN#/OBI
L5	23678	SEA FILE=CAPLUS ABB=ON	OSMOTIC?/OBI
L6	3359	SEA FILE=CAPLUS ABB=ON	PHYSIOLOGIC?/OBI(L)SALINE/OBI
L8	24	SEA FILE=CAPLUS ABB=ON	GELATIN#/OBI(W)LIKE/OBI
L9	44086	SEA FILE=CAPLUS ABB=ON	COLLOID#/OBI
L10	2310	SEA FILE=CAPLUS ABB=ON	BLOOD SUBSTITUTES/CT
L13	2602	SEA FILE=CAPLUS ABB=ON	PLASMA/OBI(L)SUBSTITUT?/OBI
L14	8	SEA FILE=CAPLUS ABB=ON	L8 AND (L2 OR (L4 OR L5 OR L6) OR (L9 OR L10) OR L13)

L2	1756	SEA FILE=CAPLUS ABB=ON	PLASMA/OBI(L)EXPANDER#/OBI
L4	28541	SEA FILE=CAPLUS ABB=ON	RECOMB?/OBI(L)PROTEIN#/OBI
L5	23678	SEA FILE=CAPLUS ABB=ON	OSMOTIC?/OBI
L6	3359	SEA FILE=CAPLUS ABB=ON	PHYSIOLOGIC?/OBI(L)SALINE/OBI
L9	44086	SEA FILE=CAPLUS ABB=ON	COLLOID#/OBI
L10	2310	SEA FILE=CAPLUS ABB=ON	BLOOD SUBSTITUTES/CT
L13	2602	SEA FILE=CAPLUS ABB=ON	PLASMA/OBI(L)SUBSTITUT?/OBI
L19	63402	SEA FILE=CAPLUS ABB=ON	COLLAGEN#/OBI
L20	1	SEA FILE=CAPLUS ABB=ON	L19 AND L4 AND (L2 OR L5 OR L6 OR L9 OR L10 OR L13)

L2	1756	SEA FILE=CAPLUS ABB=ON	PLASMA/OBI(L)EXPANDER#/OBI
L5	23678	SEA FILE=CAPLUS ABB=ON	OSMOTIC?/OBI
L6	3359	SEA FILE=CAPLUS ABB=ON	PHYSIOLOGIC?/OBI(L)SALINE/OBI
L9	44086	SEA FILE=CAPLUS ABB=ON	COLLOID#/OBI
L10	2310	SEA FILE=CAPLUS ABB=ON	BLOOD SUBSTITUTES/CT
L13	2602	SEA FILE=CAPLUS ABB=ON	PLASMA/OBI(L)SUBSTITUT?/OBI
L21	74	SEA FILE=CAPLUS ABB=ON	RECOMB?/OBI(L)GELATIN#/OBI
L22	4	SEA FILE=CAPLUS ABB=ON	L21 AND (L2 OR L5 OR L6 OR L9 OR L10 OR L13)

=> s l14 or l20 or l22

L91 9 L14 OR L20 OR L22

=> fil embase; d que l87; d que l89

FILE 'EMBASE' ENTERED AT 12:20:57 ON 17 JUN 2005

FILE COVERS 1974 TO 16 Jun 2005 (20050616/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
L76          5803 SEA FILE=EMBASE ABB=ON  GELATIN/CT
L77           154 SEA FILE=EMBASE ABB=ON  RECOMBINANT/CT
L78         17627 SEA FILE=EMBASE ABB=ON  RECOMBINANT PROTEIN/CT
L84             9 SEA FILE=EMBASE ABB=ON  L76/MAJ AND (L77 OR L78)
L85             7 SEA FILE=EMBASE ABB=ON  (L77/MAJ OR L78/MAJ) AND L76
L87             2 SEA FILE=EMBASE ABB=ON  L84 AND L85


L76          5803 SEA FILE=EMBASE ABB=ON  GELATIN/CT
L77           154 SEA FILE=EMBASE ABB=ON  RECOMBINANT/CT
L78         17627 SEA FILE=EMBASE ABB=ON  RECOMBINANT PROTEIN/CT
L84             9 SEA FILE=EMBASE ABB=ON  L76/MAJ AND (L77 OR L78)
L85             7 SEA FILE=EMBASE ABB=ON  (L77/MAJ OR L78/MAJ) AND L76
L86            14 SEA FILE=EMBASE ABB=ON  L84 OR L85
L89             3 SEA FILE=EMBASE ABB=ON  L86 AND (PICHIA)


=> s l87 or l89

L92             4 L87 OR L89

=> fil medl; d que l65; d que l66; d que l71

FILE 'MEDLINE' ENTERED AT 12:20:59 ON 17 JUN 2005

 FILE LAST UPDATED: 16 JUN 2005 (20050616/UP). FILE COVERS 1950 TO DATE.

 On December 19, 2004, the 2005 MeSH terms were loaded.

 The MEDLINE reload for 2005 is now available. For details enter HELP
 RLOAD at an arrow promt (=>). See also:

    http://www.nlm.nih.gov/mesh/
    http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html

 OLDMEDLINE now back to 1950.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2005 vocabulary.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


L59            12 SEA FILE=MEDLINE ABB=ON  GELATIN-LIKE
L60         10666 SEA FILE=MEDLINE ABB=ON  (PLASMA OR BLOOD)(2A)(EXPAN? OR
                  SUBSTITUT?)
L61          6930 SEA FILE=MEDLINE ABB=ON  BLOOD SUBSTITUTES/CT OR PLASMA
                  SUBSTITUTES/CT
L62          2808 SEA FILE=MEDLINE ABB=ON  HEMODILUTION/CT
L64        109664 SEA FILE=MEDLINE ABB=ON  RECOMBINANT PROTEINS/CT
L65             0 SEA FILE=MEDLINE ABB=ON  L59 AND ((L60 OR L61 OR L62) OR L64)
```

```
L60       10666 SEA FILE=MEDLINE ABB=ON  (PLASMA OR BLOOD)(2A)(EXPAN? OR
                SUBSTITUT?)
L61        6930 SEA FILE=MEDLINE ABB=ON  BLOOD SUBSTITUTES/CT OR PLASMA
                SUBSTITUTES/CT
L62        2808 SEA FILE=MEDLINE ABB=ON  HEMODILUTION/CT
L63        5041 SEA FILE=MEDLINE ABB=ON  GELATIN/CT
L64      109664 SEA FILE=MEDLINE ABB=ON  RECOMBINANT PROTEINS/CT
L66           0 SEA FILE=MEDLINE ABB=ON  L63 AND L64 AND (L60 OR L61 OR L62)


L63        5041 SEA FILE=MEDLINE ABB=ON  GELATIN/CT
L64      109664 SEA FILE=MEDLINE ABB=ON  RECOMBINANT PROTEINS/CT
L71           2 SEA FILE=MEDLINE ABB=ON  L64(L)BI/CT AND L63/MAJ
```

Subheading BI = biosynthesis

```
=> => dup rem l71,l91,l92,l90
FILE 'MEDLINE' ENTERED AT 12:21:35 ON 17 JUN 2005

FILE 'CAPLUS' ENTERED AT 12:21:35 ON 17 JUN 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'EMBASE' ENTERED AT 12:21:35 ON 17 JUN 2005
COPYRIGHT (C) 2005 Elsevier Inc. All rights reserved.

FILE 'BIOSIS' ENTERED AT 12:21:35 ON 17 JUN 2005
Copyright (c) 2005 The Thomson Corporation

FILE 'BIOTECHDS' ENTERED AT 12:21:35 ON 17 JUN 2005
COPYRIGHT (C) 2005 THE THOMSON CORPORATION

FILE 'WPIDS' ENTERED AT 12:21:35 ON 17 JUN 2005
COPYRIGHT (C) 2005 THE THOMSON CORPORATION
PROCESSING COMPLETED FOR L71
PROCESSING COMPLETED FOR L91
PROCESSING COMPLETED FOR L92
PROCESSING COMPLETED FOR L90
L93           17 DUP REM L71 L91 L92 L90 (7 DUPLICATES REMOVED)
                 ANSWERS '1-2' FROM FILE MEDLINE
                 ANSWERS '3-11' FROM FILE CAPLUS
                 ANSWERS '12-13' FROM FILE EMBASE
                 ANSWERS '14-15' FROM FILE BIOSIS
                 ANSWER '16' FROM FILE BIOTECHDS
                 ANSWER '17' FROM FILE WPIDS

=> d iall 1-2; d ibib ed abs hitind 3-11; d iall 12-17; fil hom

L93  ANSWER 1 OF 17     MEDLINE on STN                  DUPLICATE 4
ACCESSION NUMBER:   2003543173     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 14623401
TITLE:              Recombinant collagen and gelatin for drug delivery.
AUTHOR:             Olsen David; Yang Chunlin; Bodo Michael; Chang Robert;
                    Leigh Scott; Baez Julio; Carmichael David; Perala Maritta;
                    Hamalainen Eija-Riitta; Jarvinen Marko; Polarek James
CORPORATE SOURCE:   FibroGen, Inc., 225 Gateway Boulevard, South San Francisco,
                    CA 94080, USA.. dolsen@fibrogen.com
CONTRACT NUMBER:    R01 AR45879 (NIAMS)
```

SOURCE: Advanced drug delivery reviews, (2003 Nov 28) 55 (12) 1547-67. Ref: 104
Journal code: 8710523. ISSN: 0169-409X.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200405
ENTRY DATE: Entered STN: 20031119
Last Updated on STN: 20040520
Entered Medline: 20040519

ABSTRACT:
The tools of recombinant protein expression are now being used to provide recombinant sources of both collagen and gelatin. The primary focus of this review is to discuss alternatives to bovine collagen for biomedical applications. Several recombinant systems have been developed for production of human sequence collagens. Mammalian and insect cells were initially used, but were thought to be too costly for commercial production. Yeast have been engineered to express high levels of type I homotrimer and heterotrimer and type II and type III collagen. Co-expression of collagen genes and cDNAs encoding the subunits of prolyl hydroxylase has lead to the synthesis of completely hydroxylated, thermostable collagens. Human types I and III collagen homotrimers have been expressed in transgenic tobacco plants, while transgenic mice have been engineered to produce full-length type I procollagen homotrimer as well as a alpha2 (I) homotrimeric mini-collagen. Most recently, a transgenic silkworm system was used to produce a fusion protein containing a collagenous sequence. Each of these transgenic systems holds great promise for the cost-effective large-scale production of recombinant human collagens. As seen in other recombinant expression systems, transgenic silkworms, tobacco, and mice lack sufficient endogenous prolyl hydroxylase activity to produce fully hydroxylated collagen. In mice and tobacco, this was overcome by over-expression of prolyl hydroxylase, analogous to what has been done in yeast and insect cell culture. In addition to recombinant alternatives to bovine collagen, other sources such as fish and sponge collagen are discussed briefly. Recombinant gelatin has been expressed in Pichia pastoris and Hansenula polymorpha in both non-hydroxylated and hydroxylated forms. Pichia was shown to be a highly productive system for gelatin production. The recombinant gelatins produced in yeast are of defined molecular weight and physio-chemical properties and represent a new biomaterial not previously available from animal sources. Genetic engineering has made great progress in the areas of recombinant collagen and gelatin expression, and there are now several alternatives to bovine material that offer an enhanced safety profile, greater reproducibility and quality, and the ability of these materials to be tailored to enhance product performance.

CONTROLLED TERM:
Animals
Chemistry, Pharmaceutical
*Collagen
Collagen: BI, biosynthesis
Collagen: CH, chemistry
Collagen: GE, genetics
*Drug Carriers
Drug Carriers: CH, chemistry
***Gelatin**
Gelatin: CH, chemistry
Gelatin: GE, genetics
Humans
Organisms, Genetically Modified
Recombinant Proteins: BI, biosynthesis

Searched by Barb O'Bryen, STIC 2-2518

Recombinant Proteins: CH, chemistry
Recombinant Proteins: GE, genetics
Research Support, U.S. Gov't, P.H.S.
CAS REGISTRY NO.: 9000-70-8 (Gelatin); 9007-34-5 (Collagen)
CHEMICAL NAME: 0 (Drug Carriers); 0 (Recombinant Proteins)

L93 ANSWER 2 OF 17 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 1999387091 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10455232
TITLE: High-yield secretion of recombinant gelatins by Pichia pastoris.
AUTHOR: Werten M W; van den Bosch T J; Wind R D; Mooibroek H; de Wolf F A
CORPORATE SOURCE: Agrotechnological Research Institute (ATO-DLO), Bornsesteeg 59, 6708 PD Wageningen, The Netherlands.. m.w.t.werten@ato.dlo.nl
SOURCE: Yeast (Chichester, England), (1999 Aug) 15 (11) 1087-96. Journal code: 8607637. ISSN: 0749-503X.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199910
ENTRY DATE: Entered STN: 19991101
Last Updated on STN: 19991101
Entered Medline: 19991020

ABSTRACT:
Recombinant non-hydroxylated gelatins based on mouse type I and rat type III collagen sequences were secreted from the methylotrophic yeast Pichia pastoris, using the Saccharomyces cerevisiae alpha-mating factor prepro signal. Proteolytic degradation could be minimized to a large extent by performing fermentations at pH 3.0 and by adding casamino acids to the medium, even though gelatin is extremely susceptible to proteolysis due to its open, unfolded structure. Proteolytic cleavage at specific mono-arginylic sites, by a putative Kex2-like protease, could be successfully abolished by site-directed mutagenesis of these sites. Production levels as high as 14.8 g/l clarified both were obtained, using multicopy tranformants. To our knowledge, this represents the highest level of heterologous protein secretion reported to date for P. pastoris.

CONTROLLED TERM: Amino Acid Sequence
Collagen: ME, metabolism
DNA: CH, chemistry
DNA Primers: CH, chemistry
Electrophoresis, Polyacrylamide Gel
Fermentation
Gelatin: AN, analysis
***Gelatin: SE, secretion**
Genetic Vectors: CH, chemistry
Hydrogen-Ion Concentration
Molecular Sequence Data
Mutagenesis, Site-Directed
Pichia: GE, genetics
Pichia: GD, growth & development
*Pichia: ME, metabolism
Plasmids: CH, chemistry
*Proprotein Convertases
Recombinant Proteins: AN, analysis
***Recombinant Proteins: BI, biosynthesis**
Recombinant Proteins: SE, secretion

Saccharomyces cerevisiae: GE, genetics
*Saccharomyces cerevisiae Proteins
Sequence Analysis
Subtilisins: CH, chemistry
Transformation, Genetic
CAS REGISTRY NO.: 9000-70-8 (Gelatin); 9007-34-5 (Collagen); 9007-49-2 (DNA)
CHEMICAL NAME: 0 (DNA Primers); 0 (Genetic Vectors); 0 (Plasmids); 0 (Recombinant Proteins); 0 (Saccharomyces cerevisiae Proteins); EC 3.4.- (Proprotein Convertases); EC 3.4.21.- (Subtilisins); EC 3.4.21.61 (KEX2 protein, S cerevisiae)

L93 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2005:275732 CAPLUS
DOCUMENT NUMBER: 142:322688
TITLE: Use of **recombinant gelatin-like proteins** as blood **plasma expanders** and compositions suitable for **plasma substitution**
INVENTOR(S): Bouwsrta, Jan Bastiaan; Toda, Yuzo
PATENT ASSIGNEE(S): Fuji Photo Film B.V., Neth.
SOURCE: Jpn. Kokai Tokkyo Koho, 23 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2005082584	A2	20050331	JP 2003-320045	20030911
PRIORITY APPLN. INFO.:			JP 2003-320045	20030911

ED Entered STN: 31 Mar 2005
AB The invention relates to compns. containing a recombinant gelatin-like protein as a plasma expander, suitable for use for plasma substitution, wherein the gelatin-like protein can be a monomer, dimer, trimer or tetramer of a human recombinant gelatin-like protein having a mol. weight of 10,000-50,000 D and an isoelec. point of < 8.
IC ICM A61K038-17
ICS A61P007-08; A61P037-08; C07K014-78
CC 63-3 (Pharmaceuticals)
ST **recombinant** human **gelatin like protein plasma expander**
IT **Proteins**
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**recombinant**; use of **recombinant gelatin-like proteins** as blood **plasma expanders** and compns. suitable for **plasma substitution**)
IT Blood **plasma**
Blood substitutes
Human
Protein sequences
(use of **recombinant gelatin-like proteins** as blood **plasma expanders** and compns. suitable for **plasma substitution**)
IT **Gelatins**, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(use of **recombinant gelatin-like proteins** as blood **plasma expanders** and compns. suitable for **plasma substitution**)

IT 848267-59-4P 848267-66-3P 848267-67-4P 848267-75-4P
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; use of **recombinant gelatin-like proteins** as blood **plasma expanders** and compns. suitable for **plasma substitution**)

L93 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2004:551003 CAPLUS
DOCUMENT NUMBER: 141:102781
TITLE: Coating a microcarrier bead with gelatine or **gelatine-like** protein for cell culture support
INVENTOR(S): Bouwstra, Jan Bastiaan; Van Es, Andries Johannes Jozef; Toda, Yuzo
PATENT ASSIGNEE(S): Fuji Photo Film B.V., Neth.
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004056976	A2	20040708	WO 2003-NL922	20031223
WO 2004056976	A3	20041021		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 2002-80539 A 20021223
ED Entered STN: 09 Jul 2004
AB The invention relates to a support for culturing cells, in particular to microcarriers coated with gelatine or gelatine-like proteins. Such microcarriers serve as support for culturing anchorage dependent cells. In particular the invention relates to a process for the preparation of a cell culture support comprising the step of coating a microcarrier bead with gelatine or gelatine-like protein, said gelatine or gelatine-like protein having a mol. weight of .apprx.40 kDa to .apprx.200 kDa. Preparation of microcarrier beads coated by human recombinant gelatin-like protein Hu-3 is described. Cell attachment and cell culture protocol for gelatine or gelatine-like protein coated microcarriers is provided.
IC ICM C12N005-00
CC 9-16 (Biochemical Methods)
ST **gelatine like** protein microcarrier bead coating cell culture support
IT Proteins
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified);

PRP (Properties); RCT (Reactant); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(Hu-3; coating microcarrier bead with gelatine or **gelatine-like** protein for cell culture support)

IT Porous materials
Spheres
(beads; coating microcarrier bead with gelatine or **gelatine-like** protein for cell culture support)

IT Animal tissue culture
Coating materials
Coating process
(coating microcarrier bead with gelatine or **gelatine-like** protein for cell culture support)

IT Gelatins, biological studies
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation); USES (Uses)
(coating microcarrier bead with gelatine or **gelatine-like** protein for cell culture support)

IT Crosslinking
(**gelatine-like** protein Hu-3 immobilization using; coating microcarrier bead with gelatine or **gelatine-like** protein for cell culture support)

IT Proteins
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**gelatine-like**; coating microcarrier bead with gelatine or **gelatine-like** protein for cell culture support)

IT Proteins
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); PNU (Preparation, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(immobilized, gelatine or **gelatine-like** protein; coating microcarrier bead with gelatine or **gelatine-like** protein for cell culture support)

IT Electric charge
Immobilization, molecular or cellular
Molecular weight
(of gelatine or **gelatine-like** protein; coating microcarrier bead with gelatine or **gelatine-like** protein for cell culture support)

IT Protein sequences
(of **gelatine-like** protein Hu-3; coating microcarrier bead with gelatine or **gelatine-like** protein for cell culture support)

IT Repeat motifs (protein)
(of **gelatine-like** protein; coating microcarrier bead with gelatine or **gelatine-like** protein for cell culture support)

IT Human
(**recombinant gelatin-like protein** Hu-3 of; coating microcarrier bead with gelatine or **gelatine-like protein** for cell culture support)

IT 719776-13-3P, Protein Hu-3 (synthetic human)
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); PRP (Properties); RCT (Reactant); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(amino acid sequence; coating microcarrier bead with gelatine or **gelatine-like** protein for cell culture support)

IT 9003-53-6, Polystyrene
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(beads; coating microcarrier bead with gelatine or **gelatine-like** protein for cell culture support)

IT 51-35-4, Hydroxyproline 147-85-3, Proline, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(content, in **gelatine-like** protein; coating microcarrier bead with gelatine or **gelatine-like** protein for cell culture support)

IT 135605-29-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(crosslinking agent; coating microcarrier bead with gelatine or **gelatine-like** protein for cell culture support)

L93 ANSWER 5 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2004:213311 CAPLUS
DOCUMENT NUMBER: 140:259088
TITLE: Use of **recombinant gelatin-like proteins** as **plasma expanders** and compositions suitable for **plasma substitution**
INVENTOR(S): Bouwstra, Jan Bastiaan; Toda, Yuzo
PATENT ASSIGNEE(S): Fuji Photo Film B.V., Neth.
SOURCE: Eur. Pat. Appl., 31 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1398324	A1	20040317	EP 2002-78745	20020911
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
US 2005101531	A1	20050512	US 2003-658989	20030910
PRIORITY APPLN. INFO.:			EP 2002-78745 A	20020911

ED Entered STN: 17 Mar 2004

AB The invention relates to compns. suitable for plasma substitution comprising as a plasma expander a recombinant gelatin-like protein. Characteristic is that the gelatin-like protein can be a monomer or a polymer like a dimer, trimer or a tetramer of a human recombinant gelatin-like protein having an isoelec. point of less than 8. The resulting gelatin-like proteins provide a method to control the clearance rate of a plasma expander by its mol. weight Preferably the gelatin-like proteins have a low hydroxyproline content which prevents the composition from gelling and thus allows the use of high-mol. weight proteins in order to establish a suitable colloid osmotic pressure. An addnl. advantage of the gelatin-like proteins is that these avoid the risk of anaphylactic shock that exists in conjunction with the use of com. available prepns.

IC ICM C07K014-78
ICS A61K038-39; A61P007-08
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 3
ST **recombinant** human **gelatin like protein plasma expander**
IT **Gelatins**, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(-like **protein**; use of **recombinant gelatin -like proteins** as **plasma expanders** and compns. suitable for **plasma substitution**)

IT Blood **plasma**
(**expander**; use of **recombinant gelatin-like proteins** as **plasma expanders** and compns. suitable for **plasma substitution**)

IT **Proteins**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**gelatin-like protein** Hu-1; use of **recombinant gelatin-like proteins** as **plasma expanders** and compns. suitable for **plasma substitution**)

IT **Proteins**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**gelatin-like protein** Hu-3; use of **recombinant gelatin-like proteins** as **plasma expanders** and compns. suitable for **plasma substitution**)

IT **Proteins**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**gelatin-like protein** Hu-4; use of **recombinant gelatin-like proteins** as **plasma expanders** and compns. suitable for **plasma substitution**)

IT **Proteins**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**gelatin-like protein** Hu-deam; use of **recombinant gelatin-like proteins** as **plasma expanders** and compns. suitable for **plasma substitution**)

IT **Osmotic** pressure
(oncotic, **recombinant gelatin-like protein** with function for; use of **recombinant gelatin-like proteins** as **plasma expanders** and compns. suitable for **plasma substitution**)

IT Human
Physiological saline solutions
Protein engineering
Protein sequences
(use of **recombinant gelatin-like proteins** as **plasma expanders** and compns. suitable for **plasma substitution**)

IT 671251-44-8P, **Protein** Hu-1 (synthetic human) 671251-45-9P, **Protein** Hu-3 (synthetic human) 671251-46-0P, **Protein** Hu-4 (synthetic human) 671251-47-1P, **Protein** Hu-deam (synthetic human)
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP

(Preparation); USES (Uses)
(amino acid sequence; use of **recombinant gelatin-like proteins** as **plasma expanders** and compns. suitable for **plasma substitution**)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L93 ANSWER 6 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 5
ACCESSION NUMBER: 2002:693122 CAPLUS
DOCUMENT NUMBER: 137:237689
TITLE: **Recombinant gelatin-like proteins** for use as **plasma expanders**
INVENTOR(S): Bouwstra, Jan Bastiaan; Toda, Yuzo
PATENT ASSIGNEE(S): Fuji Photo Film B.V., Neth.
SOURCE: Eur. Pat. Appl., 14 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
EP 1238675	A1	20020911	EP 2001-200837		20010306
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
WO 2002070000	A1	20020912	WO 2002-NL147		20020306
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
EP 1368056	A1	20031210	EP 2002-702968		20020306
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2004524322	T2	20040812	JP 2002-569172		20020306
US 2005119170	A1	20050602	US 2003-469747		20020306
PRIORITY APPLN. INFO.:			EP 2001-200837	A	20010306
			WO 2002-NL147	W	20020306

ED Entered STN: 13 Sep 2002
AB The invention relates to compns. suitable for plasma substitution comprising as a plasma expander a recombinant gelatin-like protein. Characteristic is that the gelatin-like protein essentially is free of hydroxyproline. This absence of hydroxyproline prevents the composition from gelling and thus allows the use of high-mol. weight proteins in order to establish a suitable colloid osmotic pressure. Specific advantage of the gelatin-like proteins is that these avoid the risk of anaphylactic shock that exists in conjunction with the use of com. available prepns.
IC ICM A61K038-39
ICS A61P007-08
CC 63-3 (Pharmaceuticals)
ST blood **plasma expander** gelatin protein hydroxyproline absence
IT **Gelatins**, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(-like **proteins**; **recombinant** hydroxyproline-free **gelatin-like proteins** for use as **plasma expanders**)

IT **Colloids**
(**osmotic** function of; **recombinant** hydroxyproline-free **gelatin-like proteins** for use as **plasma expanders**)

IT **Blood substitutes**
Buffers
Molecular cloning
Molecular weight distribution
Physiological saline solutions
Protein sequences
(**recombinant** hydroxyproline-free **gelatin-like proteins** for use as **plasma expanders**)

IT Phosphates, biological studies
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**recombinant** hydroxyproline-free **gelatin-like proteins** for use as **plasma expanders**)

IT 51-35-4, Hydroxyproline 56-87-1, Lysine, biological studies 1190-94-9, Hydroxylysine
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(absence of; **recombinant** hydroxyproline-free **gelatin-like proteins** for use as **plasma expanders**)

IT 457968-10-4
RL: PAC (Pharmacological activity); PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(amino acid sequence; **recombinant** hydroxyproline-free **gelatin-like proteins** for use as **plasma expanders**)

IT 50-21-5, Lactic acid, biological studies 50-99-7, Glucose, biological studies 71-52-3, Bicarbonate, biological studies 7439-95-4, Magnesium, biological studies 7440-09-7, Potassium, biological studies 7440-70-2, Calcium, biological studies
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**recombinant** hydroxyproline-free **gelatin-like proteins** for use as **plasma expanders**)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L93 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 6
ACCESSION NUMBER: 2001:360037 CAPLUS
DOCUMENT NUMBER: 134:362228
TITLE: **Recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof
INVENTOR(S): Chang, Robert C.; Kivirikko, Kari I.; Neff, Thomas B.; Olsen, David R.; Polarek, James W.
PATENT ASSIGNEE(S): Fibrogen, Inc., USA
SOURCE: PCT Int. Appl., 137 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001034646	A2	20010517	WO 2000-US30791	20001110
WO 2001034646	A3	20011206		
WO 2001034646	C2	20021121		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2388477	AA	20010517	CA 2000-2388477	20001110
EP 1232181	A2	20020821	EP 2000-978455	20001110
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003516730	T2	20030520	JP 2001-537357	20001110
BR 2000015508	A	20030610	BR 2000-15508	20001110
US 2003064074	A1	20030403	US 2002-232175	20020830
PRIORITY APPLN. INFO.:			US 1999-165114P P	19991112
			US 2000-204437P P	20000515
			US 2000-710249 B1	20001110
			WO 2000-US30791 W	20001110

ED Entered STN: 18 May 2001

AB The present invention relates to recombinant gelatins and compns. thereof, and methods of producing and using the same. Human gelatins with discrete fragments of the α1(I) chain of human type I collagen is produced using a yeast multi-gene recombinant expression system. Specific fragments of cDNA for α1(I) chain from human type I collagen is cloned for the expression in Pichia pastoris which is also transformed with genes for the α or β subunit of human prolyl 4-hydroxylase, which is used to improve the stability of the recombinant gelatins. Well-defined, highly homogenous gelatin fragments ranging in size from 6-65 kDa are produced, which can support cell attachment activity, have lower level endotoxin contamination, and are proteolytically more stable. The peptide profile of thermal, acid, and enzymic hydrolysis anal., and antigenicity of these recombinant gelatins are studied. This presents unsurpassed flexibility in terms of the size and biophys. properties of the gelatin that can be used for pharmaceutical or industrial applications.

IC ICM C07K014-78
ICS C12N015-12; C12P021-02; C07K016-18; C12P021-02; C12R001-84

CC 3-2 (Biochemical Genetics)
Section cross-reference(s): 1, 17, 42, 45, 63

ST **recombinant gelatin** genetic engineering pharmaceutical industrial application; **Collagen** type I alpha1 chain gene Pichia transformation **gelatin**

IT Films
(-forming agent, comprising **recombinant gelatin**; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)

IT Hydrolysis
(acid; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)
IT Adhesives
Colloids
(agent, comprising **recombinant gelatin**; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)
IT Complexing agents
(binding agent, comprising **recombinant gelatin**; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)
IT Hydroxylation
(biol., Thermal; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)
IT Fungi
Insect (Insecta)
Plant cell
(cells of, expression host; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)
IT Animal tissue culture
Chemical industry
Cosmetics
Drug delivery systems
Emulsifying agents
Encapsulants
Food
Gelation agents
Laboratories
Plant tissue culture
Stabilizing agents
Test kits
Thickening agents
(comprising **recombinant gelatin**; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)
IT Fat substitutes
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(comprising **recombinant gelatin**; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)
IT Coating materials
(edible, comprising **recombinant gelatin**; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)
IT Toxins
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(endotoxins, contamination in **recombinant gelatin** prepared in yeast; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and

industrial applications thereof)

IT Hydrolysis
(enzymic; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)

IT Blood **plasma**
(**expander**, comprising **recombinant gelatin** ; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)

IT Animal cell
Yeast
(expression host; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)

IT Gene, animal
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(for **collagen** type I α chain; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)

IT Epitopes
(from **recombinant gelatins**; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)

IT **Protein** sequences
(**gelatins** derived from human type I **collagen** α1 chain; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)

IT Coating materials
(graft, comprising **recombinant gelatin**; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)

IT Capsules
(hard gel or soft gel, comprising **recombinant gelatin** ; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)

IT Komagataella pastoris
(host; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)

IT Photography
(materials, comprising **recombinant gelatin**; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)

IT Carriers
(microcarriers, comprising **recombinant gelatin**; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)

IT Cosmetics
(moisturizers, agent, comprising **recombinant gelatin** ; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)

IT Medical goods

(plug, comprising **recombinant gelatin**; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)

IT **Collagens**, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(procollagens, for **recombinant gelatins** preparation; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)

IT Post-translational processing
(proteolytic processing; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)

IT Molecular cloning
Vaccines
(**recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)

IT **Gelatins**, biological studies
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**recombinant**, derived from human type I **collagen** α1 chain; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)

IT Medical goods
(sponges, comprising **recombinant gelatin**; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)

IT **Proteins**, general, preparation
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(supplement, comprising **recombinant gelatin**; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)

IT Diet
(supplements, comprising **recombinant gelatin**; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)

IT Antibodies
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(to **recombinant gelatin**; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)

IT **Collagens**, biological studies
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(type I, α1 chain, **recombinant gelatins** derived from; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)

IT **Collagens**, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(type II, for **recombinant gelatins** preparation; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)

IT **Collagens**, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(type III, for **recombinant gelatins** preparation; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)

IT **Collagens**, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(type IV, for **recombinant gelatins** preparation; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)

IT **Collagens**, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(type IX, for **recombinant gelatins** preparation; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)

IT **Collagens**, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(type V, for **recombinant gelatins** preparation; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)

IT **Collagens**, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(type VI, for **recombinant gelatins** preparation; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)

IT **Collagens**, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(type VII, for **recombinant gelatins** preparation; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)

IT **Collagens**, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(type VIII, for **recombinant gelatins** preparation; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)

IT **Collagens**, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(type X, for **recombinant gelatins** preparation;

recombinant gelatins derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)

IT **Collagens**, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(type XI, for **recombinant gelatins** preparation; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)

IT **Collagens**, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(type XII, for **recombinant gelatins** preparation; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)

IT **Collagens**, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(type XIII, for **recombinant gelatins** preparation; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)

IT **Collagens**, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(type XIV, for **recombinant gelatins** preparation; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)

IT **Collagens**, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(type XIX, for **recombinant gelatins** preparation; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)

IT **Collagens**, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(type XV, for **recombinant gelatins** preparation; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)

IT **Collagens**, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(type XVI, for **recombinant gelatins** preparation; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)

IT **Collagens**, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(type XVII, for **recombinant gelatins** preparation; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)

IT **Collagens**, biological studies

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(type XVIII, for **recombinant gelatins** preparation; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)

IT **Collagens**, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(type XX, for **recombinant gelatins** preparation; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)

IT Signal peptides
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(used for **recombinant gelatin** expression in yeast; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)

IT **Colloids**
(volume replacement material, comprising **recombinant gelatin**; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)

IT 339371-03-8P, **Gelatin** (human 10kDa) 339371-04-9P, **Gelatin** (human 23kDa) 339371-05-0P, **Gelatin** (human 45kDa) 339371-06-1P, **Gelatin** (human 9kDa) 339371-07-2P, **Gelatin** (human 18-kilodaton) 339371-08-3P, **Gelatin** (human 22kDa) 339371-09-4P, **Gelatin** (human 50-kilodalton) 339371-10-7P, **Gelatin** (human 8kDa) 339371-11-8P, **Gelatin** (human 15kDa) 339371-12-9P, **Gelatin** (human 37kDa) 339371-13-0P, **Gelatin** (human 22kDa) 339371-14-1P, **Gelatin** (human 65kDa) 339371-15-2P, **Gelatin** (human) 339371-16-3P, **Gelatin** (human 33-kilodalton) 339371-17-4P, **Gelatin** (human) 339371-18-5P, **Gelatin** (human) 339525-54-1P, **Gelatin** (human 5kDa) 339525-55-2P, **Gelatin** (human 5kDa)
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)

IT 9028-06-2
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(gene for, for in vivo hydrolysis of **recombinant gelatin** expressed in yeast; **recombinant gelatins** derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)

IT 339373-01-2, 1: PN: WO0134801 SEQID: 1 unclaimed DNA 339373-02-3
339373-03-4, 3: PN: WO0134801 SEQID: 3 unclaimed DNA 339373-04-5
339373-05-6, 5: PN: WO0134801 SEQID: 5 unclaimed DNA 339373-06-7
339373-07-8 339373-08-9 339373-09-0 339373-10-3 339373-11-4
339373-12-5 339373-13-6 339373-14-7 339373-15-8
RL: PRP (Properties)
(unclaimed nucleotide sequence; **recombinant gelatins**

derived from type I **collagen** α1 chain, and pharmaceutical and industrial applications thereof)

L93 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:441507 CAPLUS
DOCUMENT NUMBER: 133:81505
TITLE: Silver halide photographic emulsion containing **recombinant gelatin-like protein**
INVENTOR(S): De Wolf, Anton; Werten, Marc Willem Theodoor; Wisselink, Hendrik Wouter; Jansen-Van Den Bosch, Tanja Jacoba; Toda, Yuzo; Van Heerde, Georg Valentino; Bouwstra, Jan Bastiaan
PATENT ASSIGNEE(S): Fuji Photo Film B.V., Neth.
SOURCE: Eur. Pat. Appl., 12 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1014176	A2	20000628	EP 1999-204382	19991217
EP 1014176	A3	20000802		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6150081	A	20001121	US 1998-219849	19981223
US 2003229205	A1	20031211	US 1998-219849	19981223
			US 2003-342331	20030115
PRIORITY APPLN. INFO.:			US 1998-219849 A	19981223
			NL 1997-1007908 A	19971224
			US 2000-617842 B1	20000717

ED Entered STN: 30 Jun 2000
AB The invention provides a nonnatural gelatin-like protein prepared by genetic engineering and having a mol. weight of from about 2500 to about 100,000 and an amino acid sequence comprising more than 4 different amino acids. The invention also provides a tabular silver halide photog. emulsion containing the gelatin-like protein as a peptizer. Tabular grains account for more than 75% of the total grain-projected area of the photog. emulsion, and the silver halide grains are nucleated in the presence of a nucleation peptizer and thereafter grown in the presence of a growth peptizer, wherein either the nucleation peptizer or the growth peptizer can be the recombinant gelatin-like protein.
IC ICM G03C001-005
ICS G03C001-047; C07K014-78
CC 74-2 (Radiation Chemistry, Photochemistry, and Photographic and Other Reprographic Processes)
IT Peptides, uses
Proteins, specific or class
RL: TEM (Technical or engineered material use); USES (Uses)
(nonnatural, nonhelical **gelatin-like**; as peptizers for silver halide photog. emulsions)
IT Photographic emulsions
(tabular; containing **recombinant gelatin-like proteins** as peptizers)

L93 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1957:77048 CAPLUS
DOCUMENT NUMBER: 51:77048
ORIGINAL REFERENCE NO.: 51:13906g-i,13907a-e

TITLE: Unsaturated organic compounds
INVENTOR(S): Shacklett, Comer D.
PATENT ASSIGNEE(S): E. I. du Pont de Nemours & Co.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2777872		19570115	US	

ED Entered STN: 22 Apr 2001

AB This invention pertains to processes of preparing N-substituted amides of unsubstituted acrylic acids containing a betaine group and certain of their derivs. Thus, a stirred ice-cooled solution of CH2:CMeCONH(CH2)3NMe2 in Et2O 212, acetone 238, or EtCOMe 242 treated dropwise during 1.5-2 h. with propiolactone 1 part in 2/3 of the quantity of the same solvent employed for the amino amide, the mixture allowed to stand 24 h., and the resulting crystalline N-(3-methacrylamidopropyl)-N,N-dimethyl-β-aminopropionate betaine (I) filtered off in a moisture-free atmospheric, washed several times with fresh portions of acetone or Et2O, and dried in the absence of moist air, preferably in vacuo. I, m. 116-16.5°, is obtained in 95% yield. Similarly CH2:CMeCONHCH2CH2NMe2 yields 95% N-(2-methacrylamidoethyl)-N,N-dimethyl-β-aminopropionate betaine, m. 108-8.5°; (3-acrylamidopropyl)dimethylamine gives 83% N-(3-acrylamidopropyl)-N,N-dimethyl-β-aminopropionate betaine, m. 118-21°; and CH2:CHCONHCH2CH2NMe2 yields N-(2-acrylamidoethyl)-N,N-dimethyl-β-aminopropionate betaine, m. 111-12°. By use of the proper amino amide and halogenated ester various betaine derivs. are obtained. Thus, CH2:CMeCONHCH2CH2NMe2 with ClCH2CO2Me gave 75% [CH2:CMeCONHCH2CH2N(CH2CO2Me)Me2] Cl, m. 155-7°. Similarly were produced the following betaine derivs. [CH2:CMeCONHCH2CH2N(CH2CO2R)R2']X (R, R', X, and m.p. given): Me, Me, Cl, 155-7°; Et, Me, Cl, 126-7°; Me, Me, Br, 147-8°; Et, Me, Br, 106-7°; Me, Me, I, 106-7°; Et, Me, I, 92-3°; Me, Et, Cl, 148-9° (decomposition); Me, Et, Br, 134-5°; Et, Et, Br, 121-2°; Me, Et, I, 97-8°; Et, Et, I, 114-15°. [CH2:CMeCONHCH2CH2N(CHMeCO2R)R2]X: Et, Me, Br, 110-11°; Me, Me, I, 114-14.5°. [CH2:CMeCONHCH2CH2CH2N(CH2CO2R)R2']X: Me, Me, Cl, 129-30°; Et, Me, Cl, 147-8°; Me, Me, Br, 131-2°; Et, Me, Br, 125-6°; Me, Me, I, 123-4°; Et, Me, I, 96-7°; Me, Et, Br, 167.5-8.0°; Et, Et, Br, 114-15°; Me, Et, I, 159-60°; Et, Et, I, 129-30°. [CH2:CMeCONHCH2CH2CH2N(CHMeCO2R)R2']X: Et, Me, Br, 93-4°; Me, Me, I, 119-20°. [CH2:CHCONHCH2CH2N(CH2CO2R)R2']X: Me, Me, Cl, 149-50° (decomposition); Me, Me, Br, 129-30°; Et, Me, Br, 75-6°; Et, Me, I, 79-81°; Me, Et, Cl, 155-6°; Me, Et, Br, 145-6°; Et, Et, Br, 97-8°; Et, Et, I, 107-7.5°; Me, Me, Cl, 149-50° (decomposition). [CH2:CHCONHCH2CH2N(CHMeCO2Et)Me2]I, m. 90-1°, was also prepared [CH2:CHCONH(CH2)3N(CH2CO2R)R2']X: Me, Me, Br, 150-0.5°; Et, Me, Br, 132.5-3.0°; Me, Me, I, 137-8°; Et, Et, Br, 122-3°; Et, Et, I, 111-12°. [CH2:CHCONH(CH2)3N(CHMeCO2R)R2']X: Et, Me, Br, 143-4°; Me, Me, I, 117-18°. To form betaines from betaine derivs. 0.1 part betaine derivative in 100 parts H2O is treated with sufficient base to give a solution pH 10.0-12.0, kept at that pH at least 1 h., then enough acid added to change the pH to 6.5-7.5. This gives betaine-containing compds. To obtain betaines a suitable polymerization inhibitor is added to a neutral solution of the betaine-containing compds., the H2O evaporated in vacuo at room temperature, the residue

dried in vacuo over a strong desiccating agent, and extracted with a suitable solvent, e.g., MeCN, at 40-80°; on cooling, the extract deposits the crystalline betaine. A list is given of 12 betaines which have been obtained by hydrolysis. These compds. are capable of addition-polymerization, of forming polymers that produce hard films, and are readily polymerizable to colloids having hydrophilic properties that are useful as gelatin substitutes.

CC 10 (Organic Chemistry)

IT **Gelatin**
(-**like** compds., betaine polymers as)

IT **Colloids**
(hydrophilic, from betaine polymers)

L93 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1957:99298 CAPLUS
DOCUMENT NUMBER: 51:99298
ORIGINAL REFERENCE NO.: 51:17984i
TITLE: Unsaturated organic compounds
PATENT ASSIGNEE(S): E. I. du Pont de Nemours & Co.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 757285		19560919	GB	

ED Entered STN: 22 Apr 2001
AB See U.S. 2,777,872 (C.A. 51, 13906g).
CC 10 (Organic Chemistry)
IT **Gelatin**
(-**like** compds., betaine polymers as)
IT **Colloids**
(hydrophilic, from betaine polymers)

L93 ANSWER 11 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1957:99297 CAPLUS
DOCUMENT NUMBER: 51:99297
ORIGINAL REFERENCE NO.: 51:17984h-i
TITLE: ε-Caprolactam
INVENTOR(S): Kobayashi, Eiji; Hattori, Saburo
PATENT ASSIGNEE(S): Mitsubishi Chemical Industries Co.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 30006112		19550831	JP	

ED Entered STN: 22 Apr 2001
AB ε-Aminocaproic acid (20 g.) and 180 g. MeOH is placed in an autoclave, air replaced with H, the mixture shaken at 220° 3 h., cooled, and distilled to yield 15.2 g. ε-caprolactam, b4 113-14°, and 0.2 g. Me ε-aminocaproate. The use of EtOH instead of MeOH, and N instead of H gave similar results.
CC 10 (Organic Chemistry)
IT **Gelatin**
(-**like** compds., betaine polymers as)

IT **Colloids**
(hydrophilic, from betaine polymers)

L93 ANSWER 12 OF 17 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2001294123 EMBASE
TITLE: Secreted production of a custom-designed, highly hydrophilic gelatin in **Pichia** pastoris.
AUTHOR: Werten M.W.T.; Wisselink W.H.; Jansenvan den Bosch T.J.; De Bruin E.C.; De Wolf F.A.
CORPORATE SOURCE: M.W.T. Werten, Agrotechnol. Res. Inst. (ATO BV), Bornsesteeg 59, 6708 PD Wageningen, Netherlands. m.w.t.werten@ato.wag-ur.nl
SOURCE: Protein Engineering, (2001) Vol. 14, No. 6, pp. 447-454.
Refs: 56
ISSN: 0269-2139 CODEN: PRENE
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20010906
Last Updated on STN: 20010906

ABSTRACT: A custom-designed, highly hydrophilic gelatin was produced in ***Pichia*** pastoris. Secreted production levels in single-copy transformants were in the range 3-6 g/l of clarified broth and purification to near homogeneity could be accomplished by differential ammonium sulfate precipitation. Despite the fact that gelatins are highly susceptible to proteolysis because of their unfolded structure, the recombinant protein was shown to be fully intact by SDS-PAGE, N-terminal sequencing, gel filtration chromatography and mass spectrometry. Owing to its highly hydrophilic nature, the migration of the synthetic gelatin in SDS-PAGE was severely delayed. Esterification of the carboxylic amino acid side chains resulted in normal migration. The high polarity of the synthetic gelatin also accounts for its negligible surface activity in water at concentrations up to 5 % (w/v), as determined by tensiometry. Circular dichroism spectrometry showed that the non-hydroxylated gelatin did not form triple helices at 4°C. The spectrum was even more representative of the random coil conformation than the spectrum of natural nonhydroxylated gelatins.

CONTROLLED TERM: Medical Descriptors:
*protein secretion
Pichia pastoris
hydrophilicity
protein synthesis
protein purification
precipitation
protein degradation
protein folding
polyacrylamide gel electrophoresis
protein structure
amino terminal sequence
sequence analysis
gel filtration chromatography
mass spectrometry
esterification
surface property

concentration (parameters)
circular dichroism
triple helix
protein conformation
nonhuman
article
priority journal
Drug Descriptors:
***gelatin: EC, endogenous compound**
recombinant protein
CAS REGISTRY NO.: (gelatin) 9000-70-8

L93 ANSWER 13 OF 17 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2000205546 EMBASE
TITLE: In vitro and in vivo evaluation of gelatin-chondroitin sulphate hydrogels for controlled release of antibacterial proteins.
CORPORATE SOURCE: J. Feijen, Department Chemical Technology, Institute Biomedical Technology, University of Twente, Drienerlolaan 5, 7500 Enschede. j.feijen@ct.utwente.nl
SOURCE: Biomaterials, (2000) Vol. 21, No. 17, pp. 1763-1772.
Refs: 15
ISSN: 0142-9612 CODEN: BIMADU
PUBLISHER IDENT.: S 0142-9612(00)00064-8
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 027 Biophysics, Bioengineering and Medical Instrumentation
037 Drug Literature Index
039 Pharmacy
004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20000706
Last Updated on STN: 20000706

ABSTRACT: Chemically cross-linked gelatin-chondroitin sulphate (ChS) hydrogels, impregnated in Dacron, were evaluated as drug delivery systems for antibacterial proteins. The gelatin-chondroitin sulphate gels, plain or impregnated in Dacron, were cross-linked with a water-soluble carbodiimide (EDC) and N-hydroxysuccinimide (NHS). The release of lysozyme and recombinant thrombocidin (rTC-1), an antibacterial protein derived from human blood platelets, from the gelatin-ChS gels in Dacron in phosphate-buffered saline at 37°C was determined, and compared to the release from gelatin gels in Dacron and plain gelatin-ChS gels. The incorporation of chondroitin sulphate into gelatin gels, caused a marked increase in lysozyme loading capacity, and a slower release rate. The relative release profiles for rTC-1 and lysozyme were equal for cross-linked gelatin as well as for cross-linked gelatin-ChS gels. Furthermore, rTC-1 showed no loss of antibacterial activity after 1 week of release. The lysozyme concentration profiles in the samples and in the surrounding medium as a function of time were calculated using mathematical solutions for Ficks second law of diffusion for a semi-infinite composite medium, which is a schematic representation of a slab in a surrounding medium. The biocompatibility and degradation of the Dacron matrices impregnated with gelatin-ChS gels was studied after implantation in subcutaneous pockets in rats. Chemically cross-linked gelatin-ChS gels showed a mild tissue reaction, and almost complete degradation within 18 weeks of implantation. Copyright (C) 2000 Elsevier Science Ltd.

CONTROLLED TERM: Medical Descriptors:

*hydrogel
*controlled release formulation
*tissue reaction
*drug delivery system
*biocompatibility
*cross linking
in vitro study
in vivo study
drug release
antibacterial activity
drug implantation
biodegradation
human
nonhuman
animal experiment
controlled study
human cell
article
priority journal
Drug Descriptors:
***gelatin**
*chondroitin sulfate
*protein: PD, pharmacology
*protein: PR, pharmaceutics
*antiinfective agent: PD, pharmacology
*antiinfective agent: PR, pharmaceutics
*antiinfective agent: AD, drug administration
*antiinfective agent: SC, subcutaneous drug administration
*dacron
*lysozyme: PD, pharmacology
*lysozyme: PR, pharmaceutics
*lysozyme: AD, drug administration
*lysozyme: SC, subcutaneous drug administration
***recombinant protein: PD, pharmacology**
***recombinant protein: PR, pharmaceutics**
***recombinant protein: AD, drug administration**
***recombinant protein: SC, subcutaneous drug administration**
CAS REGISTRY NO.: (gelatin) 9000-70-8; (chondroitin sulfate) 9007-28-7, 9082-07-9; (protein) 67254-75-5; (dacron) 60527-88-0; (lysozyme) 9001-63-2
COMPANY NAME: Fluka (Switzerland); Labaz (France); Sigma (United States); Sorin (Italy)

L93 ANSWER 14 OF 17 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:198958 BIOSIS
DOCUMENT NUMBER: PREV200200198958
TITLE: Determination of the average percent von Willebrand factor-cleaving protease (vWF-CP) activity in donor plasma.
AUTHOR(S): Kelley, Violet A. [Reprint author]; Hillyer, Krista L.; Roush, Karen R.; Long, Eric L.; Barclay, Sheilagh B.; Duncan, Alexander; Hillyer, Christopher D.
CORPORATE SOURCE: Department of Pathology and Laboratory Medicine, Emory University School of Medicine, Atlanta, GA, USA
SOURCE: Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 539a-540a. print.
Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 1. Orlando, Florida, USA. December 07-11, 2001. American Society of Hematology.

Searched by Barb O'Bryen, STIC 2-2518

CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 20 Mar 2002
Last Updated on STN: 20 Mar 2002

ABSTRACT:The etiology of acquired thrombotic thrombocytopenic purpura (TTP) has been linked to antibody inhibition of the metalloprotease enzyme (vWF-CP) which cleaves large von Willebrand Factor multimers into smaller, usable fragments. In our laboratory we have developed a modified assay (an ELISA based on the differential binding activity of vWF multimers to collagen) to determine vWF-CP activity in plasma. The average percent activity of vWF-CP has not been established for our methodology. We therefore sought to define an average percent activity of vWF-CP by assaying 97 plasma samples which were aliquots of FFP units from normal blood donors. First, the plasma samples were treated with 93mM barium chloride to dissolve existing large vWF multimers and vWF substrate was added after the first incubation. The vWF substrate was prepared from pooled FFP, and the native vWF-CP activity was abolished by the addition of 15 mM EDTA and 2mM Pefabloc, which were removed by dialysis prior to incubation with the samples. The samples were then transferred to collagen-coated plates that were prepared by adding 3ug/ml **recombinant** human **collagen** Type III in PBS to CovaLink plates, 250 uL/well for (4 hours), followed by blocking with 250ul 2.5% BSA, for 15 minutes. Following incubation, HRP-labelled anti-vWF conjugate was added, followed by substrate development. Finally, the optical density of the plasma samples on the collagen plate was read spectrophotometrically at 450nm. Calibration curves were created for each run of approximately eight plasma samples using pooled FFP in dilutions of 1:5 to 1:320. A 1:20 dilution was arbitrarily given the value of 100% activity (calibration curve plotted using the equation y=aebx). All 97 plasma samples were tested in duplicate at this dilution. The average activity for all of the samples was 97% with a standard deviation of 60%. There was no statistically significant difference in average percent vWF-CP activity among plasma samples from group A, B, O or AB donors. Using this method, the activity of vWF-CP in normal donor plasma appears to have a wide range (37-157%) with an average of 97%.

CONCEPT CODE: General biology - Symposia, transactions and proceedings 00520
Clinical biochemistry - General methods and applications 10006
Biochemistry studies - General 10060
Biochemistry studies - Proteins, peptides and amino acids 10064
Enzymes - General and comparative studies: coenzymes 10802
Pathology - Therapy 12512
Blood - Blood and lymph studies 15002
Blood - Blood cell studies 15004
Blood - Blood, lymphatic and reticuloendothelial pathologies 15006
Bones, joints, fasciae, connective and adipose tissue - Pathology 18006
Pharmacology - Clinical pharmacology 22005
Pharmacology - Blood and hematopoietic agents 22008
INDEX TERMS: Major Concepts
Clinical Chemistry (Allied Medical Sciences); Enzymology (Biochemistry and Molecular Biophysics); Hematology (Human Medicine, Medical Sciences)
INDEX TERMS: Parts, Structures, & Systems of Organisms
plasma: blood and lymphatics

Searched by Barb O'Bryen, STIC 2-2518

INDEX TERMS: Diseases
thrombotic thrombocytopenic purpura: blood and lymphatic disease, connective tissue disease, drug therapy
Purpura, Thrombotic Thrombocytopenic (MeSH)
INDEX TERMS: Chemicals & Biochemicals
EDTA; FFP [fresh frozen plasma]: hematologic-drug, **plasma** volume **expander**; Pefabloc; barium chloride; **recombinant** human **collagen** type III; von Willebrand factor [vWF]; von Willebrand factor-cleaving protease
INDEX TERMS: Miscellaneous Descriptors
Meeting Abstract; Meeting Poster
ORGANISM: Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human: blood donor, patient
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates
REGISTRY NUMBER: 60-00-4 (EDTA)
30827-99-7 (Pefabloc)
10361-37-2 (barium chloride)

L93 ANSWER 15 OF 17 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:198957 BIOSIS
DOCUMENT NUMBER: PREV200200198957
TITLE: von Willebrand factor-cleaving protease (vWF-CP) activity in S-59-treated donor plasma.
AUTHOR(S): Hillyer, Krista L. [Reprint author]; Kelley, Violet A. [Reprint author]; Roush, Karen S. [Reprint author]; Long, Eric L. [Reprint author]; Barclay, Sheilagh B. [Reprint author]; Duncan, Alexander [Reprint author]; Roback, John D. [Reprint author]; Hillyer, Christopher D. [Reprint author]
CORPORATE SOURCE: Department of Pathology and Laboratory Medicine, Emory University School of Medicine, Atlanta, GA, USA
SOURCE: Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 539a. print.
Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 1. Orlando, Florida, USA. December 07-11, 2001. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 20 Mar 2002
Last Updated on STN: 20 Mar 2002
ABSTRACT:Pathogen inactivation technology represents a major improvement in blood product safety against transmission of infectious diseases. Donor plasma treated (tx) with psoralen compounds such as amotosalen HCl (S-59) and UVA light (HelinxTM technology) has excellent pathogen-inactivating efficacy. This increased safety against infectious disease transmission is particularly important for those patients (pts) who receive large quantities of fresh frozen plasma (FFP). For example, large volumes of FFP are routinely used as replacement fluid during therapeutic plasma exchange (PE) in pts with thrombotic thrombocytopenic purpura (TTP). The etiology of acquired TTP has

been linked to antibody inhibition of an enzyme, von Willebrand factor-cleaving protease (vWF-CP), that cleaves pathogenic, large vWF multimers into normal, small fragments. PE has two major benefits in the treatment of TTP: it decreases the levels of large, pathogenic vWF multimers and antibody inhibitor by removing pt plasma, and it replenishes vWF-CP via the infusion of normal donor plasma (typically FFP). We sought to determine whether donor plasma treated with S-59 retains vWF-CP activity similar to that found in FFP, in order to demonstrate whether S-59-tx donor plasma is an equally effective replacement fluid for PE in pts with TTP. Thus, to determine if the S-59 process adversely affects enzyme activity, we tested 97 paired FFP samples, pre- and post-S-59-treatment, by ELISA based on the differential binding activity of vWF multimers to collagen. The samples were treated with 93mM barium chloride to dissolve existing large vWF multimers. After this incubation, vWF substrate (prepared from pooled FFP with its native protease activity abolished by the addition of 15 mM EDTA and 2mM Pefabloc, removed by dialysis prior to sample incubation) was added. The pre- and post-S-59-tx donor plasma samples were transferred to collagen-coated plates (prepared by adding 3ug/ml **recombinant** human **collagen** Type III in PBS to CovaLink plates, 250 uL/well(4 hours), followed by blocking with 250ul 2.5% BSA (15 minutes, RT)). Following incubation, HRP-labeled anti-vWF conjugate was added, followed by substrate development. Finally, the optical density of the samples on the collagen plate was spectrophotometrically measured at 450nm. Calibration curves were created for each run of 8 plasma samples using pooled normal FFP in dilutions of 1:5 to 1:320. A 1:20 dilution was arbitrarily given the value of 100% vWF-CP activity (calibration curve plotted using y=aebx)and all plasma samples were tested in duplicate at this dilution. The average pre- and post-S-59 treatment vWF-CP activity values were 76.54% and 77.22%, respectively (p=0.81, mean SD=23.38%, mean R2=0.881, n=97). Previous studies in our laboratory have demonstrated that vWF-CP activity varies in normal donor plasma, with the normal range using our assay of 40-150% activity. As our results show that there is no statistically significant difference in mean vWF-CP activity in S-59-treated donor plasma as compared with FFP, we conclude that S-59-treated donor plasma is likely an equally suitable PE replacement fluid in TTP. Clinical studies utilizing S-59-tx donor plasma as replacement fluid for PE in TTP patients are currently underway and will provide more information as to the efficacy of S-59-tx donor plasma in the treatment of this disease.

CONCEPT CODE:
General biology - Symposia, transactions and proceedings 00520
Clinical biochemistry - General methods and applications 10006
Biochemistry studies - General 10060
Biochemistry studies - Proteins, peptides and amino acids 10064
Enzymes - General and comparative studies: coenzymes 10802
Pathology - Therapy 12512
Blood - Blood and lymph studies 15002
Blood - Blood cell studies 15004
Blood - Blood, lymphatic and reticuloendothelial pathologies 15006
Pharmacology - General 22002
Pharmacology - Clinical pharmacology 22005
Pharmacology - Blood and hematopoietic agents 22008

INDEX TERMS:
Major Concepts
Clinical Chemistry (Allied Medical Sciences); Enzymology (Biochemistry and Molecular Biophysics); Hematology (Human Medicine, Medical Sciences); Pharmacology

INDEX TERMS:
Parts, Structures, & Systems of Organisms
plasma: blood and lymphatics

Searched by Barb O'Bryen, STIC 2-2518

INDEX TERMS: Diseases
thrombotic thrombocytopenia: blood and lymphatic disease, drug therapy
INDEX TERMS: Chemicals & Biochemicals
EDTA; Pefabloc; amotosalen hydrochloric acid [S-59]: hematologic-drug, radiosensitizer-drug; barium chloride; collagen; fresh frozen plasma: hematologic-drug, **plasma** volume **expander**; **recombinant** human **collagen** type III; von Willebrand factor [vWF]; von Willebrand factor-cleaving protease
INDEX TERMS: Miscellaneous Descriptors
Meeting Abstract; Meeting Poster
ORGANISM: Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human: patient
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates
REGISTRY NUMBER: 60-00-4 (EDTA)
30827-99-7 (Pefabloc)
10361-37-2 (barium chloride)

L93 ANSWER 16 OF 17 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2003-03126 BIOTECHDS
TITLE: New composition comprising a repetitive polymer containing alternating blocks of sequences that promote protein crystallization and sequences that are elastin, collagen or keratin-like elements, useful for in vivo **drug** delivery;
recombinant elastin, **collagen** or keratin-like element for disease therapy
AUTHOR: CAPPELLO J; STEDRONSKY E R
PATENT ASSIGNEE: CAPPELLO J; STEDRONSKY E R
PATENT INFO: US 2002045567 18 Apr 2002
APPLICATION INFO: US 1997-806029 24 Feb 1997
PRIORITY INFO: US 1997-806029 24 Feb 1997; US 1997-806029 24 Feb 1997
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2002-681318 [73]
ABSTRACT: DERWENT ABSTRACT:
NOVELTY - A composition (C1) comprising: (a) a protein polymer of at least 15kDa which comprises alternating blocks of at least 2 units each of a sequence of 3-30 amino acids which promotes protein crystallization, and an amino acid sequence which is an elastin-like element, a collagen-like element or a keratin-like element; and (b) a biologically active substance.
DETAILED DESCRIPTION - A composition (C1) comprising: (a) a protein polymer of at least 15kDa which comprises alternating blocks of at least 2 units each of a sequence of 3-30 amino acids which promotes protein crystallization, and an amino acid sequence which is an elastin-like element, a collagen-like element or a keratin-like element; and (b) a biologically active substance. The composition acquires a non-liquid form under physiological conditions. INDEPENDENT CLAIMS are also included for the following: (1) delivering a

biologically active substance to a localized site in vivo, comprising administering C1, where the biologically active substance is delivered from the non-liquid to the localized site; and (2) altering the physical dimensions of a body tissue of a mammal, comprising administering a C1.

BIOTECHNOLOGY - Preferred Composition: The amino acid sequence which promotes protein crystallization is preferably GAGAGS or SGAGAG. It is preferably repeated between 2 to 16 times per alternating block. The amino acid sequence which is an elastin, collagen or keratin-like element is preferably S1, S2, S3 or S4. VPGG (S1); APGVGV (S2); GXGVP (S3); or VPGXG (S4); where X = is valine, lysine, histidine, glutamic acid, arginine, aspartic acid, serine, tryptophan, tyrosine, phenylalanine, leucine, glutamine, asparagine, cysteine or methionine, more preferably valine or lysine. Most preferably the protein polymer comprises the amino acid sequence selected from S5-S12. ((VPGVG)8(GAGAGS)8)12 (S5); ((VPGVG)12(GAGAGS)8)9 (S6); ((VPGVG)16(GAGAGS)8)8 (S7); ((VPGVG)32(GAGAGS)8)5 (S8); ((VPGVG)8(GAGAGS)6)13 (S9); ((VPGVG)8(GAGAGS)4)13 (S10); ((GVGVP)4GKGVP(GVGVP)3(GAGAGS)4)12 (S11); or (GAGAGS(GVGVP)4GKGVP(GVGVP)3(GAGAGS)2)12 (S12). The biologically active substance is preferably a protein with a molecular weight of 350-500000 Daltons or a nucleic acid of about 60-22000 bases. The substance is preferably an anti-tumor agent, analgesic, antibiotic, anti-inflammatory compound, hormone or vaccine. Preferred Method: When delivering a biologically active substance to a localized site, delivery is over an extended time period, and comprises injecting the composition in liquid form which acquires a non-liquid form subsequent to injection. The rate at which non-liquid form is acquired decreased by addition of a compound that inhibits hydrogen bonding, preferably urea, guanidine hydrochloride, dimethyl formamide, **colloidal** gold solution, aqueous lithium bromide or formic acid. The rate is increased by adding a nucleating agent or accelerator, preferably protein polymer in pre-crystallized form, particularly SLP3 or SLP4. The protein polymer is preferably about 10-50 % (w/w) of the composition.

USE - The composition is used for the controlled release of biologically active compounds in vivo. It can also be used to alter the physical dimensions of a body tissue.

EXAMPLE - Escherichia coli strain EC3 harboring plasmids encoding each polymer were prepared using standard techniques. Each strain was then fermented using a fed-batch method and biomass for each polymer was harvested from the fermentation broth using standard techniques throughout. The protein polymers were designated SELPs. SELP8K gels were measured for controlled delivery of the protein drug Pantarin. 125I Pantarin was incorporated into 33% w/w SELP8K gel at an approximate loading concentration of 0.2 mg/ml in a buffer of 50 mM sodium citrate, 80 mM NaCl, 0. 1 M EDTA, pH 6.0. The gel was cast in a 0.5 cubic centimeter hypodermic syringe at 37 degrees Centigrade. Cylindrical sections of the gel were cut from the syringe and placed in elution tubes containing the above buffer with 0.1% gelatin, 0.05% Tween-20 at 37 degrees Centigrade. Radioactivity remaining in the gel was measured with a gamma counter. An initial rapid release of Pantarin in the first 24 hours was followed by a slow steady release of approximately 1% per day for at least 8 days.(16 pages)

CLASSIFICATION: THERAPEUTICS, Protein Therapeutics; GENETIC TECHNIQUES and APPLICATIONS, Gene Expression Techniques and Analysis; BIOMANUFACTURING and BIOCATALYSIS, Fermentation
CONTROLLED TERMS: RECOMBINANT ELASTIN, COLLAGEN, KERATIN-LIKE ELEMENT PREP., PLASMID-MEDIATED GENE TRANSFER, EXPRESSION IN ESCHERICHIA COLI, APPL. PROTEIN CRYSTALLIZATION PROMOTER, DRUG DELIVERY, DISEASE THERAPY PROTEIN BACTERIUM FERMENTATION DNA SEQUENCE PROTEIN SEQUENCE (22, 06)

L93 ANSWER 17 OF 17 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 1974-55754V [31] WPIDS
TITLE: Gelatin **blood-plasma substitutes** - based on isotonic solution of depolymerized gelatin modified with **glycol.**
DERWENT CLASS: A96 B04
PATENT ASSIGNEE(S): (TANA) TANABE SEIYAKU CO
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
JP 49014619	A	19740208	(197431)*			
JP 52018247	B	19770520	(197724)			

PRIORITY APPLN. INFO: JP 1972-55519 19720602
INT. PATENT CLASSIF.: A61K009-08
BASIC ABSTRACT:

JP 49014619 A UPAB: 19930831

Blood plasma substitutes were prepared from isotonic solns. of modified gelatin (mol. weight 20,000-60,000). The modified **gelatin** was prepduced by **recombining** depolymerized **gelatin** with glycols or by depolymerizing gelatin which had been combined with glycol.

In an example, ethylene glycol was cooled and to this was added thionyl chloride dropwise with stirring. The solution was mixed with a suspension of depolymerized gelatin (mol. weight 5000-15,000) in dimethylformamide. After stirring at room temperature the reaction mixture was poured into EtOH and precipitated gelatin was collected. The modified gelatin was dissolved in water and pH adjusted to 7.0; NaCl was added to obtain a desired tonicity. The solution was sterilized and sealed with N gas in containers.

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB
MANUAL CODES: CPI: A03-C01; A10-E05; A12-V02; B04-B04A; B12-H06

FILE 'HOME' ENTERED AT 12:22:04 ON 17 JUN 2005

=>